IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TALECRIS BIOTHERAPEUTICS, INC. and BAYER HEALTHCARE LLC, Plaintiffs, v. BAXTER INTERNATIONAL INC. and BAXTER HEALTHCARE CORPORATION, Defendants.	Civil Action No. 05-349-GMS Jury Trial Demanded **PUBLIC VERSION**
BAXTER HEALTHCARE CORPORATION, Counterclaimant, v. TALECRIS BIOTHERAPEUTICS, INC. and BAYER HEALTHCARE LLC, Counterdefendants.	

OPENING BRIEF IN SUPPORT OF SUMMARY JUDGMENT MOTION FILED BY BAXTER INTERNATIONAL INC. AND BAXTER HEALTHCARE CORPORATION

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I. INTRODUCTION

Plaintiffs primary expert witness, Dr. Jeffrey Ravetch, M.D., Ph.D., admitted he does not know the meaning of a critical claim term – "an acceptable level suitable for intravenous administration" – in the patent-in-suit. Specifically, Dr. Ravetch testified:

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[1]

In fact, no one knows what is meant by key phrases in the claims of the '191 patent. Not the inventor, or his patent attorney, or the experts hired by plaintiffs Talecris Biotherapeutics, Inc.'s and Bayer Healthcare LLC's ("Plaintiffs"). But controlling patent law requires definite boundaries for claim terms so that persons of ordinary skill in the art know how to avoid infringement. *See Geneva Pharm., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003). Where, as here, no such boundaries can be drawn, the patent must be held invalid as indefinite.

During prosecution of the '191 patent, the patentee told the United States Patent and Trademark Office what it considered the "invention" to be. When faced with indefiniteness challenges during prosecution of the '191 patent, the patentee overcame them by making limiting statements, which it has disavowed in this litigation. Now Plaintiffs offer vague and conflicting expert testimony to advance new litigation positions that serve only to confirm that the claim terms at issue are insolubly ambiguous.

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Plaintiffs' own evidence and testimony (which can raise no disputes of material fact), prove that the patent-in-suit is invalid.

II. CURRENT STATUS OF THE CASE

On June 1, 2005, Talecris Biotherapeutics, Inc. ("Talecris") filed a patent infringement action against Baxter Healthcare Corporation and Baxter International Inc. (collectively, "Baxter"), claiming infringement of United States Patent Number 6,686,191 ("the '191 patent"). An amended complaint was filed on May 5, 2006, adding a claim for damages and Bayer Healthcare LLC ("Bayer") as a plaintiff. Baxter answered and counterclaimed for a declaratory judgment that it does not infringe the '191 patent and that the patent is invalid. On November 1, 2006, Baxter filed a motion for leave to file an amended answer and counterclaim to include allegations of inequitable conduct. That motion is still pending.

Meanwhile, the parties briefed claim construction of the '191 patent and, on December 14, 2006, the Court held its claim construction hearing. The Court issued its claim construction ruling on December 28, 2006 ("Claim Construction Order"). During the claim construction process, Baxter indicated its intention to seek summary judgment of invalidity. On February 22, 2007, the Court issued a ruling permitting Baxter to file the instant motion for summary judgment on indefiniteness. A jury trial is scheduled to begin July 9, 2007.

III. SUMMARY OF THE ARGUMENT

1. All asserted claims of the '191 patent are invalid as indefinite because the claim terms "acceptable level [of anticomplement activity] suitable for intravenous administration," "increased level of anticomplement activity," and "then incubating the solution of step a)"/"the increased anticomplement activity of the solution" are insolubly ambiguous. The meaning of these terms as proposed by Plaintiffs (even in light of the

Claim Construction Order) are internally inconsistent, vague and ultimately find no support in the '191 patent.

2. Plaintiffs appear to define "acceptable level suitable for intravenous administration" to mean any level of anticomplement activity ("ACA") utilized as release limits for final products approved by the FDA, but then admit those release limits are variable, not definitive, and are subject to change. Plaintiffs further admit that the measurement of ACA varies depending upon the test used and the technician who ran it. Moreover, what is actually "acceptable" varies on a patient-by-patient basis.

3. The term "increased level of anticomplement activity" is indefinite because it either means ACA simply increased, which renders the claims of the patent nonsensical, or it means ACA increased to an "unacceptable" level, which has all the same ambiguities as the term "acceptable."

4. The phrases "then incubating the solution of step a)" and "the increased anticomplement activity of the solution" are indefinite if they would allow an undetermined and undefined number of changes to "the solution" that affect the ACA of the solution, such that "the increased anticomplement of the solution" no longer remains when "the solution of step a)" is incubated.

5. Because there are no disputed facts and Plaintiffs' experts have been unable to identify the boundaries of these claim terms, every asserted claim in the '191 patent is indefinite and summary judgment of invalidity is proper.

IV. FACTUAL BACKGROUND

A. '191 Patent

United States application serial number 08/532,211 ("U.S. application"), which ultimately led to issuance of the patent-in-suit, the '191 patent, was filed with the U.S.

Patent and Trademark Office ("Patent Office") on September 22, 1995. The '191 patent issued about eight and a half years later on February 3, 2004. The named inventor on the '191 patent is William R. Alonso. Eventually the '191 patent was assigned to Bayer Healthcare LLC.

Plaintiffs assert that Baxter infringes Claims 1, 7-12 and 15-20 of the '191 patent. Of these claims, Claim 1 is the only independent claim. The language of Claim 1, with the pertinent portions bolded, reads:

> 1. A method of treating a solution of antibodies which may have virus activity, the method comprising
>
> a) contacting the solution with a trialkylphosphate and a detergent under conditions sufficient to substantially reduce any virus activity and **resulting in an increased level of anticomplement activity**; and
>
> b) **then incubating the solution of step a)** under conditions of controlled time, pH, temperature, and ionic strength, such that **the increased anticomplement activity of the solution is reduced to an acceptable level suitable for intravenous administration**.

The asserted claims of the '191 patent are all directed to methods of treating a solution of antibodies, including an intravenously injectable immunoglobulin G solution ("IGIV"). All the methods share two important steps. The first step requires treatment with a trialkylphosphate (a solvent) and a detergent ("solvent/detergent treatment step") that "result[s] in an increased level of anticomplement activity." Rogaski Decl., Ex. 1, Claim 1, step (a). The second step requires an incubation step that reduces "the increased anticomplement activity of the solution" to "an acceptable level suitable for intravenous administration." Rogaski Decl., Ex. 1, Claim 1, step (b).

B. Claim Construction

On December 28, 2006, the Court issued its Claim Construction Order, which provides, in relevant part:

> 4. The term "increased level of anticomplement activity" is construed to have its plain and ordinary meaning.
>
> 5. The term "increased anticomplement activity of the solution" is construed to have its plain and ordinary meaning.
>
> 6. The term "then incubating the solution of step a)" is construed to mean "incubating a solution originating from step a) under conditions of controlled time, pH, temperature, and ionic strength, wherein additional steps may be performed prior to said incubating."
>
> ...
>
> 10. The term "acceptable level suitable for intravenous administration" is construed to have its plain and ordinary meaning.

Docket No. 199, pp. 2-4 (footnotes omitted). The Court did not try to define these terms further, leaving that to the evidence. But the evidence adduced by Plaintiffs proves the meaning of each of these terms is hopelessly indefinite, making it impossible to discern a "plain and ordinary meaning" for them.

V. LEGAL STANDARDS

A. Legal Standard For Summary Judgment

Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c); *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986); *see also Chimie v. PPG Indus. Inc.*, 402 F.3d 1371, 1376 (Fed. Cir.

2005); *Boyle v. County of Allegheny Pa.*, 139 F.3d 386, 393 (3d Cir. 1998). While the evidence must be viewed in the light most favorable to the non-moving party, inferences must be reasonable and cannot be drawn from omissions or deficiencies in the factual record. *See Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 587-88 (1986). "[T]he mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48 (1986). Summary judgment is proper if the factual record is so one-sided that the only reasonable resolution favors the moving party. *Id.* at 251-52. "Where the record taken as a whole could not lead a rational trier of fact to find for the non-moving party, there is no 'genuine issue for trial.'" *Matsushita*, 475 U.S. at 587 (internal citation omitted).

B. Legal Standard For Invalidity Based On Indefiniteness

Title 35 of the United States Code, Section 112, requires that a patent's specification, "… conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." 35 U.S.C. § 112 ¶ 2. This requirement is known as the "definiteness" requirement. "[T]he purpose of the definiteness requirement is to ensure that the claims delineate the scope of the invention using language that adequately notifies the public of the patentee's right to exclude." *Honeywell Int'l, Inc. v. Int'l Trade Comm'n*, 341 F.3d 1332, 1338 (Fed. Cir. 2003). "The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002); *accord Oakley, Inc. v. Sunglass Hut Int'l.*, 316 F.3d 1331, 1340 (Fed. Cir. 2003). "[A] claim is indefinite under §112 ¶ 2 if it is 'insolubly ambiguous, and no narrowing construction can

properly be adopted.'" *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342 (Fed. Cir. 2003) (citations omitted).

The *Honeywell* court invalidated a patent due to indefiniteness under facts quite similar to those present here. The invention in *Honeywell* was for producing synthetic yarn. The last claim term recited "thereby obtaining a drawn yarn with a terminal modulus of at least 20 g/d and a melting point elevation [MPE] of 10 C. to 14 C." *Honeywell*, 341 F.3d at 1335. The method used for measuring MPE was not recited in the claims. The specification provided a recognized definition for MPE, but three different methods of making the measurement existed, each providing different MPE numbers. *Id.* The three measurement methods differed in how a sample of the polyethylene terephthalate yarn (PET) was prepared. The specification did not indicate which of the PET sample preparation methods was to be used. *Id.* at 1336, 1339. Noting that the "claims, written description, and prosecution history do not mention the different sample preparation methods or provide sufficient clues to discern which methods are acceptable," the Federal Circuit held the claim "insolubly ambiguous, and hence indefinite .... [T]he claims, the written description, and the prosecution history fail to give us, as the interpreter of the claim term, any guidance as to what one of ordinary skill in the art would interpret the claim to require." *Id.* at 1340.

Claims were also found to be indefinite in the *Halliburton Energy Services, Inc. v. MI, LLC.*, 456 F. Supp. 2d 811 (E.D. Tex. 2006) case because no objective standard was provided for the claim term "fragile gel." Although the specification described a "fragile gel" as being determined by factors such as whether the gel was "easily disrupted," the *Halliburton* court noted that, "even if skilled artisans could agree on the determining factors, there is still no evidence they would agree on a particular amount or range of force, time, etc., that would make disruption or thinning 'easy' or what it means to be 'easy.'" *Id.* at 818. The patentee relied on the specification's identification of a

proprietary modified viscometer (not available to the public) as an instrument for measuring fluid properties. *Id.* But the patent provided "no specific numeric cutoff point" using this viscometer or other objective measure against which to compare the viscometer measurements. *Id.* at 820. "Although 'a patentee need not define his invention with mathematical precision to satisfy the definiteness requirement,' there must be some 'objective anchor' by which skilled artisans can identify whether they are practicing the patented invention." *Id.* (citations omitted). A number of different variables could affect the output of the viscometer measurements. Because the patent did not adequately disclose the parameters for each of those variables, "skilled artisans cannot duplicate those parameters." *Id.* at 821 (citations omitted). As the specification only provided a subjective definition for the claim term and no "objective anchor," the term "fragile gel" was found indefinite.

The *Datamize* decision is also instructive. The claim term at issue in *Datamize* was "aesthetically pleasing." *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342 (Fed. Cir. 2005). The Federal Circuit acknowledged the "ordinary meaning" of the term, but still found the term to be indefinite in the context of the patent in suit because it was "completely dependent on a person's subjective opinion. … Some objective standard must be provided in order to allow the public to determine the scope of the claimed invention." *Id.* at 1350. The Federal Circuit further advised, "When a word of degree is used the district court must determine whether the patent's specification provides some standard for measuring that degree." *Id.* at 1351, *quoting Seattle Box Co., v. Indus. Crating & Packing, Inc.* 731 F.2d 818, 826 (Fed. Cir. 1984). Most importantly, "[r]eference to undefined standards, regardless of whose views might influence the formation of those standards, fails to provide any direction to one skilled in the art attempting to determine the scope of the claimed invention." *Id.* at 1352.

VI. "ACCEPTABLE LEVEL SUITABLE FOR INTRAVENOUS ADMINISTRATION" IS INDEFINITE

Claim 1 requires that the incubation of step (b) reduce the ACA in a solution to an "acceptable level suitable for intravenous administration." Here, as in *Honeywell*, neither the method of measuring ACA (which can result in different ACA levels) nor the level of ACA that is "acceptable" is taught by the '191 patent. As in *Halliburton*, no objective measure or numeric cutoff point for "acceptability" is provided in the '191 patent. And, as in *Datamize*, the '191 patent provides no standard by which to measure "acceptability." In fact, no one associated with the '191 patent, whether during prosecution or in this litigation, has been able to define this term[2]:

- The inventor and prosecuting patent attorney admitted they did not know what this term meant; and
- None of Plaintiffs' three expert witnesses could articulate a meaningful definition of the term that defines the metes and bounds of the patent.

It is precisely when the boundaries of a claim are not understood by persons of ordinary skill in the art[3] that indefiniteness should be found. Here, not a single person has been able to identify the boundaries of Claim 1 with respect to "acceptable level suitable for intravenous administration." Without clear boundaries, potential infringers cannot determine whether or not they infringe the '191 patent, *All Dental Prodx,* 309 F.3d at 779-80, so the asserted claims are invalid.

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[2] Baxter submitted during claim construction that the only construction that could give this term definiteness would be if it required the numerical limits set forth in the '191 patent as determined by the ACA assay used by the named inventor.
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Rogaski Decl., Ex. 10, pp. 145:14-146:21. As this construction was not adopted, and no other constructions provide sufficient boundaries to Claim 1, the term is indefinite.

[3] Though the parties have offered different levels of skill in the art in this case, the claim terms at issue in this motion are indefinite regardless of which of the proposed levels of skill is applied.

A. The Patent Office Examiner, The Inventor And Prosecuting Patent Attorney Were Unable To Define "Acceptable Level"

During prosecution of the U.S. application, the Examiner initially rejected Claim 1 on the ground that the phrase "an acceptable level" of anticomplement activity was indefinite, stating, "[t]he metes and bounds of what is defined by … an 'acceptable level' cannot be determined." Docket No. 161, Joint Appendix ("JA") 35. In response, Bayer argued, "[t]he acceptable level of ACA generally depends on IGIV concentration and examples (for 5 and 10% IGIV solutions) are described in the second full paragraph of page 9." *Id.* at JA77, JA16. The second full paragraph of page 9 (also repeated in the '191 patent at Col. 5:57-64) states:

> For a 5% ISG formulation the acceptable level suitable for intravenous administration preferably would be less than about 45 CH_{50} units/mL, and more preferably less than about 30 CH_{50} units/mL. For a 10% ISG formulation the acceptable level suitable for intravenous administration preferably would be less than about 60 CH_{50} units/mL, and more preferably less than about 45 CH_{50} units/mL.

Id. at JA77; Rogaski Decl., Ex. 1, Col. 5:57-64. In response to Bayer's explanation of "acceptable level" in numerical terms based on the concentration of the IGIV, the Examiner withdrew the indefiniteness rejection, stating, "[f]urther, it was argued that 'an acceptable level' is not vague because it depends on the concentration of IGIV. … The latter argument is found to be persuasive, and the rejection based on 'an acceptable level suitable for intravenous administration' is withdrawn **based on the definition of an acceptable level found in the specification at page 9**." Docket No. 161, JA83 (emphasis added). The boundary for "an acceptable level" was thus defined by Bayer during prosecution to depend on the concentration of the IGIV sample and the particular numerical limits according to the concentration.

In the absence of this defined boundary, the claim term is meaningless, as is amply demonstrated by the inability of both the named inventor and the prosecuting patent attorney to define what is "acceptable" or "unacceptable." If neither the named inventor nor the prosecuting attorney knew what "acceptable" meant at the time the patent application was filed, one of ordinary skill in the art could not be expected to know what this term means, and whether a particular ACA level is acceptable. Dr. Alonso, the named inventor, testified:

[4]

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Rogaski Decl., Ex. 5, pp. 153:19-154:7 (emphases added).

[4] REDACTED

Rogaski Decl., Ex. 6, pp. 279:21-24.

The Bayer patent attorney who filed the application leading to the '191 patent also could not define "acceptable level:"

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Rogaski Decl., Ex. 7, pp. 106:25-107:14 and 119:25-120:9 (emphases added)

The inventor, Dr. Alonso, also confirmed that variability in the ACA test -- the "assay" -- could affect ACA results.

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Rogaski Decl., Ex. 6, pp. 280:4-282:13 (emphases added).

B. Plaintiffs' Experts Demonstrate The Indefiniteness Of "Acceptable Level"

Plaintiffs' expert, Dr. Ravetch, admitted the term "acceptable level suitable for intravenous administration" is indefinite, as he – a purported person of ordinary skill in the art – did not know what it means:

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Rogaski Decl., Ex. 8, p. 196:7-11. Plaintiffs' two other technical experts ascribe myriad different and conflicting meanings to the phrase. The simple fact that so many (inconsistent) meanings are proffered demonstrates the indefiniteness of this term. Moreover, the meanings themselves simply raise more ambiguity.

1. Acceptability Varies From Patient to Patient

Neither the '191 patent nor the Plaintiffs define a specific, measurable, amount of ACA that is, or is not, "acceptable." Plaintiffs' expert, Dr. Erwin Gelfand, stated, REDACTED

REDACTED

Rogaski

Decl., Ex. 3, p. 5.[5] REDACTED

Id. at 5.

Dr. Gelfand opined that

REDACTED

Id. at 5.

REDACTED

Id. at 5. Notably, none of these variables are discussed anywhere in the '191 patent, just as the parameters for variables were not provided in the patent at issue in the *Halliburton* case.[6] In short, there is no single level of acceptability, even for a particular commercial product. Thus, Dr. Gelfand ultimately agrees with Baxter's expert:

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Id. at p. 6 (emphasis added).

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[5] Dr. Thomas J. Kindt is one of Baxter's experts. Dr. Kindt has opined that "acceptable level suitable for intravenous administration" is indefinite if not defined as the numerical limits set forth in the '191 patent. Rogaski Decl., Ex. 18, pp. 95:5-96:1. Because the plain and ordinary meaning of this claim term is indeterminate, in evaluating the prior art, Dr. Kindt considered whether the authors or inventors of the prior art references believed their IGIV products to be suitable for intravenous administration. To this end, Dr. Kindt considered whether the products were used with patients and whether any adverse events were noted. *See, e.g., id.* at 82:7-84:24 and 92:7-97:21. As discussed herein, however, neither of those standards provides sufficient definiteness for an accused infringer to know the true boundaries of Claim 1, so cannot save Claim 1 from indefiniteness.

[6] If, in fact, these variables are necessary components of determining whether a given ACA level is "acceptable," the '191 patent must also be found invalid for lack of written description (not raised in this motion) of "acceptable level" because none of these variables are shown for any solution in the '191 patent. In addition, no infringement has been proven (though not raised in this motion) as these variables have not been addressed by Plaintiffs' experts in their infringement analysis.

Dr. Ravetch's January 31, 2007 report is the only report of any of Plaintiffs' experts that actually appeared to offer a definition of "acceptable level suitable for intravenous administration." In it, he stated,

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Rogaski Decl., Ex. 2, p. 5. Dr. Ravetch's explanation, however, simply increases the murkiness surrounding this term, as he provided no guidance regarding what REDACTED

provides no information to a manufacturer about whether or not a product that has been made and sold, but not yet administered to patients, has an "acceptable level" of ACA. Moreover, it cannot possibly be correct that whether or not a product infringes the '191 patent requires a clinical determination on a case-by-case basis.

2. Regardless Of The Standard Of "Acceptability" Chosen By Plaintiffs, The '191 Patent Remains Indefinite Because ACA Levels From Different Assays Cannot Be Compared To Any Single "Standard"

The failure of the '191 patent to identify the correct method of measuring ACA condemns "acceptable level" to insoluble ambiguity, as in the *Halliburton* case. A skilled artisan would have known that there are numerous ways of measuring ACA, that ACA levels obtained using different assays cannot be compared and that ACA levels are dependent on the particular assay used.

Rousell, *et al.*, measured ACA levels in a Bayer Corporation IGIV product using two different ACA assays. Rousell reported ACA levels measured by the Method 1 assay and by the Method 2 assay. Though the same product was being tested, and the ACA assays used were both developed by Bayer Corporation, the ACA levels determined by Method 1 and Method 2 could not be compared. Rogaski Decl., Ex. 12, p. 148-49,

Table III ("Finally, there was no correlation between the assay of AC activity by Method 1 and by Method 2 when both were used to test AC levels in IGIV, pH 4.25.").

Table III. Comparison of anticomplementary (AC) activity in ten randomly selected lots of IGIV, pH 4.25 by two AC assay methods.*

Lot Number	AC Activity (CH_{50}/ml) Method 1	Method 2
40B04	11.9	25.3
40B09	12.8 ↑	23.4 ↓
40B10A	11.9 ↓	24.7 ↑
40B11	13.5 ↑	28.6 ↑
40C04	17.2 ↑	28.5 ↓
40C05	14.3 ↓	25.5 ↓
40C07	10.4 ↓	21.6 ↓
40C08C	7.7 ↓	25.1 ↑
40C13A	8.6 ↑	26.0 ↑
40D02	8.2 ↓	25.1 ↓

* With Method 1, an acceptable AC level is considered to be below 25 units CH_{50}/ml, while with Method 2 it is considered to be below 20 units CH_{50}/ml. Pearson product-moment correlation = 0.56 ($P = 0.09$).

As can be seen from Table III of the Rousell paper, annotated above, every sample tested by Method 1 (having an upper limit of 25 units CH_{50}/mL) had an "acceptable AC level," while every sample tested by Method 2 (having an upper limit of 20 units CH_{50}/mL) did not. Additionally, an increase in ACA levels when tested by Method 1 did not always correspond to an increase in ACA levels when tested by Method 2 (as shown by the red and green highlighting and arrows in the figure above). The lack of correlation of ACA assays (as exemplified by the internal Bayer Corporation assays) is further magnified when comparing assays between **different** companies and **different** products.

The assay used to measure ACA, then, is critical to the ACA levels obtained, much as in the *Honeywell* case. Even if a numerical limit for "acceptable" ACA were set, one assay used could give "acceptable" results while a different assay could give

"unacceptable" results. By way of example, if a manufacturer produces a batch of IGIV having an ACA level of 30 CH_{50} units/mL, that company would have no way of knowing whether 30 CH_{50} units/mL is an "acceptable level suitable for intravenous administration" such that the product infringes the '191 patent. To determine whether such a product infringes, a person of ordinary skill in the art in 1995 would have looked to the '191 patent for guidance and, finding none (other than the particular "acceptable" levels recited in Column 5 obtained by an undisclosed assay), would have considered levels of ACA that others in the field have deemed "acceptable." He or she would have found **no fewer than six different standards** relating to "acceptability." For example:

- The '191 patent described limits for acceptable levels of ACA of less than about 45 CH_{50} units/mL, preferably less than about 30 CH_{50} units/mL, for 5% solutions, and less than about 60 CH_{50} units/mL, preferably less than about 45 CH_{50} units/mL, for 10% solutions. Rogaski Decl., Ex. 1, Col. 5:57-64.
- The '191 patent also stated that "IGIV preparation should have ACA levels as low as possible." Rogaski Decl., Ex. 1, Col. 5:54-55.
- The European Pharmacopoeia requires that "[t]he consumption of complement is not greater than 50 per cent (1 CH_{50} per milligram of immunoglobulin)" for immunoglobulin products sold in Europe. Rogaski Decl., Ex. 17 at BXTR068266.
- Table III in the Rousell paper showed that Method 1 had an acceptable level of 25 units CH_{50}/mL while Method 2 had an acceptable level of 20 units CH_{50}/mL. Rogaski Decl., Ex. 12, Table III, p. 148.

- The '608 patent (Tenold) identified the acceptable ACA level for an intravenously injectable ISG preparation as "greater than about 2 mg protein/C'H50 unit." Rogaski Decl., Ex. 13, Col. 6:11-27.
- The Malgras paper identified the ACA level above which IGIV solutions should be as 25 mg/2 units C'H50 (or 12.5 mg/ unit C'H50). Rogaski Decl., Ex. 14.

Consequently, an IGIV batch having an ACA level of 30 CH_{50} units/mL for a 5% solution, would alternatively be "unacceptable," "acceptable" or indeterminate depending on which of the above standards were considered (assuming the results from different assays could be compared which, as discussed above, they cannot). Specifically, 30 CH_{50} units/mL would be:

- Acceptable under the '191 patent's 45 CH_{50} units/mL standard, but unacceptable under its "preferably less than 30 CH_{50} units/mL standard."
- Indeterminate, if "as low as possible" is the standard.
- Acceptable under the European Pharmacopoeia limit of 50% for a 5% solution.
- Unacceptable under the Method 1 and Method 2 standards of Rousell (25 units CH_{50}/mL and 20 units CH_{50}/mL).
- Unacceptable under the Tenold standard of greater than about 2 mg protein/CH_{50} unit, as 30 CH_{50} units/mL would convert into approximately 1.6 mg protein/CH_{50}, which is less than 2 mg protein/CH_{50} unit.

- Unacceptable under the Malgras standard of greater than 12.5 mg/ unit CH_{50}, as 30 CH_{50} units/mL would convert into approximately 1.6 mg protein/unit CH_{50}, which is less than 12.5 mg protein/unit CH_{50}.

Based on this information, a person of ordinary skill in the art would be utterly unable to determine whether 30 CH_{50} units/mL is "an acceptable level suitable for administration." There is insufficient definition in either the '191 patent or the knowledge in the art to determine whether a given ACA level is an "acceptable level suitable for intravenous administration."

The lack of an identifiable standard in the '191 patent for "acceptable level" renders this term indefinite under *Honeywell, Datamize* and *Halliburton*. As in *Honeywell*, Claim 1 in this case recites a quantity from a measurement, *i.e.*, "acceptable [anticomplement activity] level suitable for intravenous administration," but does not provide the method used to determine "acceptable level." As in *Honeywell* and *Halliburton*, multiple methods exist for measuring anticomplement activity, these methods provide different results for the anticomplement activity level of the same sample and produce different limits for what would be considered acceptable for intravenous administration. As in *Honeywell* and *Halliburton*, the specification does not provide any detail as to which method was used to assay the samples presented in the specification or which method should be used to determine the "acceptable level" of ACA. As in *Honeywell* and *Halliburton*, the variety of methods available to measure ACA, but which have not been defined by the patentee, can result in infringement or non-infringement depending on which method is chosen. Consequently, as in *Honeywell* and *Halliburton*, the Court in this case should similarly find the term "acceptable level suitable for intravenous administration" indefinite.

3. FDA Release Limits Do Not Provide A Standard

Plaintiffs' apparently contend that if the U.S. Food and Drug Administration ("FDA") permits an IGIV product to be sold then, by definition, its ACA level must be "acceptable." This definition is both too broad and too narrow. It is too broad because, as Talecris' expert Dr. Gelfand testified, REDACTED

It is too narrow because, as Talecris' expert Dr. Pinya Cohen admits,

REDACTED

Moreover, there is no single FDA release limit for ACA levels in an IGIV product. REDACTED

In an attempt to provide some concrete context for "acceptable level,"

REDACTED

Dr. Gelfand testified

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Id. at 139:20-25. Yet, Dr. Gelfand offers no guidance as to how to determine acceptability if a product is not, or not yet, FDA approved.

Even if FDA release limits determined acceptability, this term remains indefinite.

REDACTED

. Rogaski Decl., Ex. 4, ¶¶10-11. Dr. Gelfand confirmed that

REDACTED

Rogaski Decl., Ex. 3, p. 9. Indeed, Dr. Gelfand admits that

REDACTED

Ibid. Dr. Gelfand concedes,

REDACTED

Id. at 4.

Dr. Gelfand noted that

REDACTED

Id. at 4 and 5. Because the boundary for acceptability is not fixed, a manufacturer could never know if its product has an "acceptable level" of ACA. Indeed, Dr. Gelfand testified

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Rogaski Decl., Ex. 10, pp. 123:13-124:25 and 203:5-204:23.

Of course, if a manufacturer has not yet obtained FDA approval, there is no set FDA release limit to provide any guidance to that manufacturer to determine whether or not it infringes the '191 patent.

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Rogaski Decl., Ex. 10, p. 196:3-7. Indeed, Plaintiffs have submitted no evidence whatsoever that would address this situation, which the *All Dental Prodx* court recognized is at the very heart of indefiniteness.

Moreover, Dr. Gelfand stated that the

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REDACTED Rogaski Decl., Ex. 3, p. 9 (emphasis added). In Dr. Gelfand's words, REDACTED

Id. at 5 (emphasis added).

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Rogaski Decl., Ex. 4, ¶ 16. In short, ACA limits set by the FDA for a particular product can change at any time. An ACA level that is below the release specification one day may be above it on another day. Something that is subject to "constant reevaluation" by its very nature **has no boundaries** and can only be indefinite.

Dr. Cohen acknowledged that REDACTED

Rogaski Decl., Ex. 11, pp. 54:4-55:9. Specifically, Dr. Cohen stated that REDACTED

Id. at 55:5-9. He also testified that REDACTED

Id. at 59:3-60:23. Indeed, the only way Dr. Cohen was aware of to determine if ACA is "acceptable" is to

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Id. at 60:16-23. Even then, Dr. Cohen conceded that

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Id. at 66:25-68:18.

The term "acceptable level suitable for intravenous administration" must be evaluated in the context of the '191 patent; and, there is absolutely no support in the '191 patent for "acceptable level" being tied to FDA release specifications, adverse events,

clinical determinations or patient characteristics. Moreover, as recognized by the *Datamize* court, "[r]eference to undefined standards, regardless of whose views might influence the formation of those standards, fails to provide any direction to one skilled in the art attempting to determine the scope of the claimed invention." *Datamize*, 417 F.3d at 1352. Plaintiffs' litigation reliance on FDA release limits, then, cannot save the asserted claims from indefiniteness.

4. "Adverse Events" Do Not Provide A Standard

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Even if adverse events were considered to be an indicator of acceptability, the term "acceptable level suitable for intravenous administration" would still be indefinite. Monitoring would be required on an infusion-by-infusion basis, since Plaintiffs admit that

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Id. at pp. 3 and 5. If tied to adverse events, a manufacturer would not know whether the ACA level of its product was "acceptable" unless the product was infused into a patient. Even then, if an adverse reaction occurred, the manufacturer would not necessarily know if it was due to ACA. Yet infringement

can arise simply from the manufacture of a product or its sale, as opposed to the use of a product. By tying "acceptability" to adverse events (which would only occur after manufacture, sale and use), Plaintiffs fail to provide any measure by which to determine whether or not the manufacture of a product infringes.

Even for products that are sold and used by patients, Plaintiffs never identify the type, severity or number of adverse events that would indicate the ACA level was "acceptable" or "unacceptable." For example, Dr. Gelfand testified,

REDACTED Rogaski Decl., Ex. 10, pp. 86:12-16. Given that lack of knowledge, a clinician could not know, after infusing an IGIV product into a patient, whether any adverse reactions seen were caused by ACA or were significant enough that the ACA level be deemed unacceptable, making adverse events an impossible measure of "acceptable" ACA levels. Moreover, tying "acceptable level" to adverse events would lead to the incongruous situation where a single ACA level would be "acceptable" for one patient and "unacceptable" for another patient.

While adverse events are certainly of concern to manufacturers and to patients, they are not an objective measure – or any measure at all – by which to determine whether a batch of IGIV has an "acceptable" ACA level. As such, adverse events cannot save this term from indefiniteness.

VII. "Increased Level Of Anticomplement Activity" Is Undefined

The Court construed "increased level of ACA" to have its plain and ordinary meaning. Though the Court declined to specifically construe "increased level of ACA" to require that the "increase" in ACA caused by step (a) be to an unacceptable level, Claim 1 is indefinite if the increase can simply be to an "acceptable" level. The plain language of Claim 1 requires that the incubation step (step (b)) reduce the increased ACA

"**to** an acceptable level." If the ACA was already acceptable after step (a), step (b) would have no meaning. It would be nonsensical to reduce ACA **from** an "acceptable" level **to** an "acceptable" level. Thus, this claim term is insolubly ambiguous and, therefore, indefinite.

Plaintiffs experts offer the bare – and nonsensical – opinion that

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Rogaski Decl., Ex. 3, pp. 3-4 and Rogaski Decl., Ex. 10, pp. 188:5-22. But Claim 1 does not use the term "further." The plain language of Claim 1 unambiguously requires a reduction **to** an "acceptable level." Additionally, Dr. Ravetch opines

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See, e.g., Rogaski Decl., Ex. 9, pp. 419:9-429:13. Any interpretation which does not require a reduction from an unacceptable level to an acceptable would render superfluous the claim language "such that the increased anticomplement activity of the solution is reduced to an acceptable level … ." Under such an interpretation, Claim 1 would be insolubly ambiguous.

The specification confirms that an increase just to an "acceptable" level would make no sense in the context of the '191 patent. Specifically, Bayer confirmed that the solvent/detergent treatment of step (a) "results in a product with an acceptable viral inactivation but with **unacceptably high levels of ACA**." Rogaski Decl., Ex. 1, Col. 2:6-10 (emphasis added). Even Dr. Ravetch admitted REDACTED

Rogaski Decl., Ex. 9, p. 324:20-25. Bayer makes this unequivocal by stating, "[w]e have discovered that the incubation step [*i.e.*, step (b) of claim 1] is **necessary to achieve an acceptable level of ACA** low enough to allow the [immunoglobulins] to be administered by intravenous injection." Rogaski Decl., Ex. 1,

Col. 2:31-34 (emphasis added); *see also*, *id.* at Col. 7:20-24 ("… [solvent/detergent treatment] yields a product which has **high ACA and is unsuitable for intravenous administration**."). There can be no question that, without the incubation step of step (b), the ACA level of the alleged invention would not be low enough to administer intravenously, *i.e.*, would not be "acceptable."

The prosecution history is in accord. During prosecution, Bayer tied the particular ACA level being reduced in step (b) of Claim 1 to the increased ACA caused by step (a), representing to the Patent Office that "[t]he amendments require that incubation step (b) decreases the amount of anticomplement activity (ACA) **caused** by step (a)." Docket No. 161, JA88 (emphasis added). Even so, the Examiner refused to issue the patent. On appeal, the Board of Patent Appeals found, "the claimed subject matter requires that the inactivation step result in an increase in ACA levels, and a **reduction in that claimed increase** by the incubation step to a point where the solution is suitable for intravenous use." *Id.* at JA125 (emphasis by bold added; emphasis by underlining in original). Indeed, the Decision on Appeal finds, "the claimed subject matter requires that the inactivation step result in an increase in ACA levels, and **a reduction in that claimed increase** by the incubation step to a point where the solution is suitable for intravenous use." *Id.* at JA125 (emphasis by bold added; emphasis by underlining in original). The Board also stated that treating a solution with solvent/detergent results in an increase in ACA which, even after subsequent treatment according to Tenold, purportedly does not "result in a product having acceptable ACA levels when measured immediately." *Id.* at JA127-28.

All of this evidence confirms the "increased level" after step (a) – if not unacceptable – is indefinite.

VIII. "THEN INCUBATING THE SOLUTION OF STEP A)" AND "THE INCREASED ACA OF THE SOLUTION" ARE INDEFINITE

The Court construed the term "then incubating the solution of step a)" to mean "incubating a solution originating from step a) under conditions of controlled time, pH, temperature and ionic strength, wherein additional steps may be performed prior to said incubating." Dr. Gelfand testified, REDACTED

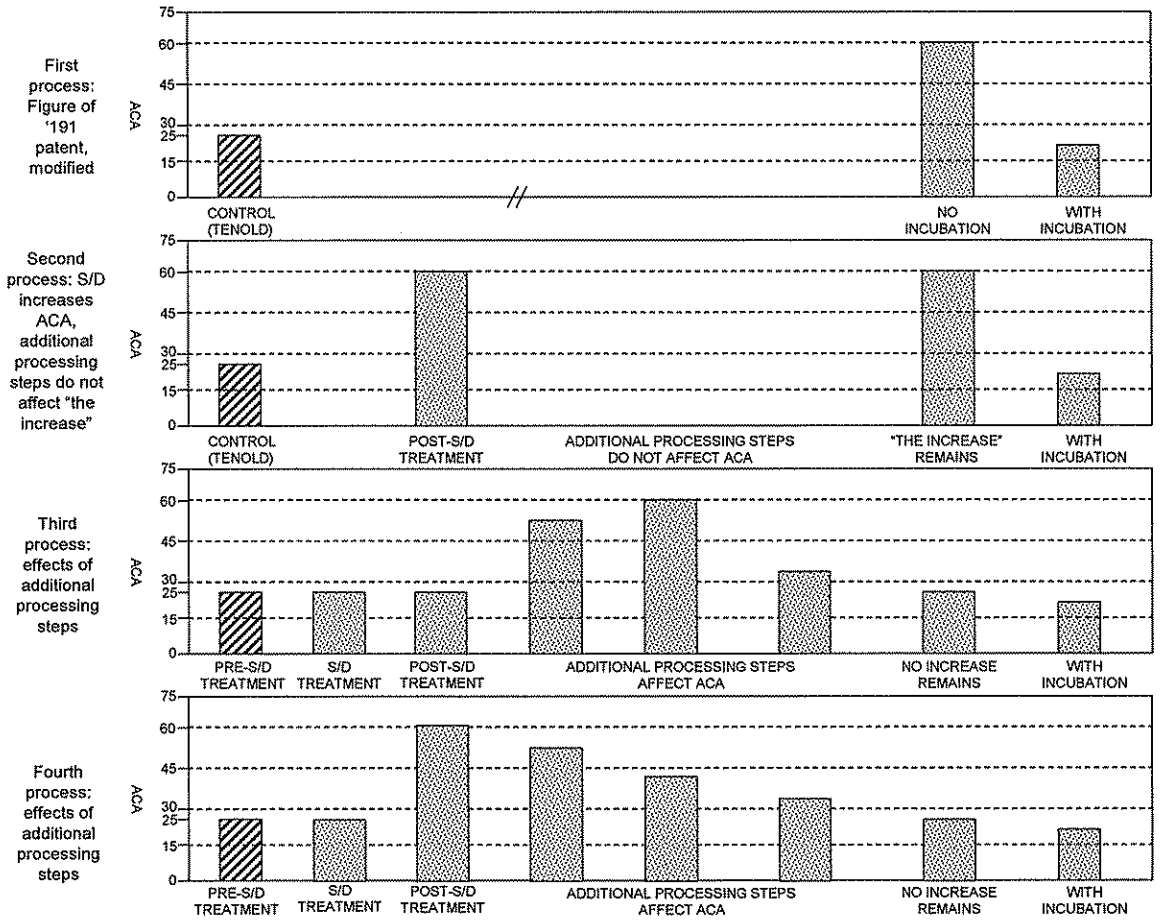
Rogaski Decl., Ex. 10, pp. 119:11-22 (emphasis added). Consistent with Dr. Gelfand's testimony and this Court's claim construction, a process may fall within Claim 1, even if it has additional processing steps between steps (a) and (b), if those additional processing steps do not affect the "increased ACA of the solution" caused by step (a). In contrast, a process having additional processing steps that do impact "the increased ACA of the solution" caused by step (a) would not fall within Claim 1 because "the increased ACA" would no longer remain when step (b) is performed.

The disclosure in Column 5 of the '191 patent reveals there could be many "solutions" "originating from step a)," including solutions that have been processed by anion exchange chromatography (which could substantially reduce ACA levels) or other handling steps that could increase ACA. *See* Rogaski Decl., Ex. 15, Col. 2:3-9 (documents reduction of ACA by anion exchange chromatography); Rogaski Decl., Ex. 16, pp. 118-121 (showing that various routine handling steps can raise ACA). Thus, these additional steps would almost certainly affect the ACA levels resulting from the solvent/detergent treatment of step (a). *See, e.g.*, Rogaski Decl., Ex. 9, pp. 429:24-431:7. As a result, if the solutions resulting from these additional processing steps have different ACA levels than the ACA level caused by the step (a) solvent/detergent treatment, the term "the increased ACA of the solution" would be nonsensical. Thus, "the increased ACA" required to be caused by step (a) and reduced by step (b) would no longer be present by the time the solution is incubated in step (b) – it would either be decreased or

would be a different increase. In other words, "**the**[7] increased ACA of the solution" would no longer be present, yet the claim language, because of its ambiguity, might be understood to find infringement nonetheless.

Four examples of different possible processes, and their effect on ACA are shown in the figures below. In the **first process**, which mirrors the Figure in the '191 patent, an "increase" in ACA is measured after solvent/detergent treatment (although the "increase" is not actually measured until after other processing steps such as diafiltration and hydrophobic chromatography). "The increase" shown by the "no incubation" sample is reduced by the step (b) incubation. In the **second process**, a similar increase is shown, but is specifically shown to be "the increase" caused by the solvent/detergent treatment step. Because the additional processing steps do not affect ACA levels, the step (b) incubation reduces "the increase" resulting from step (a). In the **third process**, however, the additional processing steps, not the solvent/detergent treatment step, cause an increase in ACA. Further, additional processing steps reduce that increase such that no increase remains to be reduced by the step (b) incubation. In the **fourth process**, an increase in ACA is caused by solvent/detergent treatment, but additional processing steps reduce the ACA such that no increase remains to be reduced by the step (b) incubation.

[7] The antecedent basis for "the increased ACA" in step (b) is "an increased level of ACA" in step (a).



Since Claim 1, as construed, could result in many "solutions" having different ACA levels than that resulting from step (a), and "the increased ACA of the solution" may no longer remain when the step (b) incubation begins, the claim terms "then incubating the solution of step a)" and "the increased anticomplement activity of the solution" are insolubly ambiguous and, therefore, Claim 1 is indefinite.

IX. CONCLUSION

The undisputed facts – from Plaintiffs, their experts, and published studies – demonstrate that the terms, "acceptable level suitable for intravenous administration," "increased level of ACA" and "then incubating the solution of step a)"/"the increased anticomplement activity of the solution" are insolubly ambiguous and, therefore,

indefinite. As there are no disputes of material fact, and indefiniteness is a question of law, summary judgment that each asserted claim is invalid as indefinite is proper.

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CERTIFICATE OF SERVICE

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